Binary Classification of Alzheimer's Disease using sMRI Imaging modality and Deep Learning

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Abstract

Alzheimer's Disease (AD) is the most common form of dementia affecting the elderly population worldwide. Many neuroimaging modalities have been used to check the detection and progression of AD of which structural Magnetic Resonance Imaging (sMRI) is an important one. The recent rise in the popularity of deep learning methods with applications in computer vision, reinforcement learning and artificial intelligence has created a resurgence in the application of these methods to the classification of AD through different imaging modalities. In this study, by utilizing the concept of transfer learning in deep learning, we propose a classification framework to differentiate subjects with Clinical Dementia Rating (CDR) of zero from subjects with CDR greater than zero by using deep learning architectures such as Xception and Inception version 3 in the Keras deep learning library. The attained validation set accuracies are as high as 99.12% for the Inception version 3 network and 97.97% for the Xception network. The presented results suggest that meaningful predictors composed of sMRI and network measures may offer the possibility for early detection of subjects in the early stages of AD.

Keywords Deep Learning, Transfer Learning, Artificial Neural Networks, Medical Imaging, Classification

Introduction

AD is the most common form of dementia characterized by a progressive degeneration of the brain in the form of accumulation of amyloid plaques, neurofibrillary tangles and loss of neurons in brain tissues [1]. Specialist services for AD are already seeing an increasing number of subjects with CDR greater than zero. Poor physical health, functional status, and depression are also associated with lower cognitive performance in the general population leading to the onset of deterioration of brain [2]. One of the primary areas of brain affected by AD is hippocampus which is responsible for forming memories hence keeping a record not

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only of our experiences, but also of their temporal structure hence performing associate chaining, positional coding and retrieving background context and thus enabling us to understand the relation between brain and behavior [3]. Other parts of brain normally affected during progression of AD are cerebral cortex, amygdala, hypothalamus, cerebellum; occipital, parietal and frontal lobes, corpus callosum, and thalamus. All these parts are directly or indirectly involved in the distinctive cognitive and behavioral operations and a defect in the performance of them augments impaired decision making [4-8].

Current diagnosis of AD relies primarily on the assessment of cognitive impairment through a battery of clinical tests as well as the practitioner's experience in the subjective evaluation of AD. However, research efforts are underway to discover an objective and correct way to identify the disease patterns of which neuroimaging is an important one. MRI is usually the modality of choice for structural brain analysis despite the popularity of other modalities such as Computed Tomography (CT) and Positron Emission Tomography (PET) [10].

Convolutional Neural Networks (CNNs) which are primarily driven by vision recognition systems inside human brain could reliably predict and decode functional MRI (fMRI) data from humans watching movies despite lacking mechanisms for temporal dynamics or feedback processing [9]. In addition to that, the ubiquitous applications of CNNs can be traced in the classification of AD using PET images [11], MRI images [12], or their counterparts 3D-CNNs [13].

In this paper, we aim to perform classification between healthy control subjects with CDR [14] of zero and subjects with CDR greater than zero using Xception [15] and Inception version 3 [16] convolutional neural network models on the cross-sectional MRI datasets from Open Access Series of Imaging Studies (OASIS) [17]. We have used the datasets from Marcia Hon et al [18] which consists of 200 subjects divided into two groups of which 100 are marked as Alzheimer's group while the rest are marked as non-Alzheimer's group.

Hardware Requirements

We run our simulations on a computer containing an NVIDIA GeForce GTX 1080 Ti Graphical Processing Unit (GPU), Intel Core i-7-7800X Central Processing Unit Correspondence Author: Yong-Kui Ma

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(CPU) running at 3.50 GHz, and 16.0 GB of installed Random Access Memory (RAM).

Software Considerations

We code our simulations in Keras [19] deep learning library. The version of Keras was 2.2.2. Keras is a high-level neural networks Application Programming Interface (API) build on top of other deep learning frameworks like Theano, Microsoft Cognitive Toolkit (CNTK), and Tensorflow. The backend to our Keras code implementation was Tensorflow version 1.10.0.

Methodology

CNNs coupled with Transfer Learning

CNNs are at the heart of modern deep learning revolution which has kickstarted after the 2012 ImageNet Large Scale Visual Recognition Challenge (ILSVRC) won by the Alexnet network. The range of applications covered by CNNs include but are not limited to object recognition, face recognition, scene labelling, image classification, action recognition, human pose estimation, document analysis, lesion detection, segmentation, image reconstruction, and natural language processing.

The core of CNNs is the operation of convolution which learns local translationally invariant patterns in the input feature space. CNNs also take advantage of the fact that visual world is fundamentally spatially hierarchical by learning spatial hierarchies of patterns in their layers of which higher layers learn incrementally complex mappings of features learned by the lower layers.

Transfer learning [20] is a popular deep learning approach aimed at reusing a model developed for a task as a starting point for a model on another task. It is a popular way of dealing with problems with comparatively little data. In this work, we have used Xception and Inception version 3 neural network models as transfer learning models for the classification of subjects between the Alzheimer's and non-Alzheimer's groups.

Inception Version 3 Model

In Inception modules, a convolutional layer attempts to learn filters to simultaneously and separately map cross-channel and spatial correlations. Inception version 3 uses Correspondence Author: Yong-Kui Ma

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the idea of replacing large size convolutional blocks with smaller sized ones, for example, a 5 x 5 convolution block is replaced by two 3 x 3 convolution blocks which results in the savings of computations. It also uses the notion of auxiliary classifiers, acting as regularizers, to combat the vanishing gradients problem by pushing the gradients to the lower layers to make them useful and improve the convergence of the network during training phase. Fig. 1 below shows a canonical Inception version 3 module.

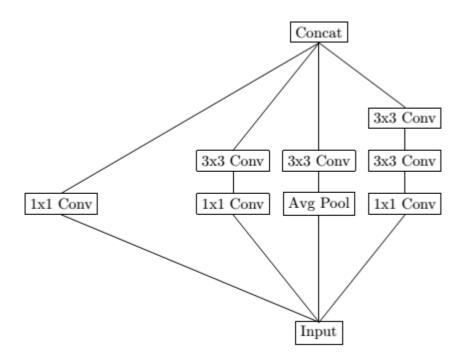


Fig. 1 A canonical Inception version 3 module

Xception Model

Xception model is a novel deep learning neural network model which gets its inspiration from Inception. It uses the idea of depthwise separable convolution which is a spatial convolution not using any non-linearity, independently performed, over channels of an input, followed by a pointwise convolution, hence projecting the channels output onto a new channel space.

Overview of Datasets

The datasets used in the study are divided into two main groups namely Alzheimer and non-Alzheimer subjects. We used 5,120 images from the two classes for training and 1,280 images for validation. We use equal number of samples from both classes Correspondence Author: Yong-Kui Ma

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for training and validation. Random samples of the images in Joint Photographic Experts Group (JPEG) format used during experiments are shown in figures Fig. 2 and Fig. 3 below.

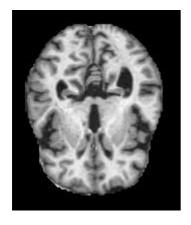


Fig. 2 Non-Alzheimer Subject

Fig. 3 Alzheimer's Subject

In addition, we use 5-fold cross-validation to split our data with each fold having the same structure of training and validation datasets as described in this section. We run our experiments in all folds.

Image Preprocessing

We rescale the images by 255 to feed our pipeline.

Building the Model

We build two models to run our simulations. The first model uses Inception version 3 model as a base model initialized with imagenet weights followed by a fully-connected layer with 256 neurons activated by rectified linear function, and a classification layer with 1 neuron activated by a sigmoid function. We use dropout with probability 0.5 to drop units in the fully-connected layer with 256 neurons.

The second model uses Xception model as a base model initialized with imagenet weights followed by a fully-connected layer with 256 neurons activated by rectified linear function, and a classification layer with 1 neuron activated by a sigmoid function. We use dropout with probability 0.5 to drop units in the fully-connected layer with 256 neurons.

Training the Models

Inception Version 3 Model

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We use binary cross-entropy as a loss function and stochastic gradient descent (SGD) as the optimization algorithm. We set the initial learning rate of SGD to 10⁻⁴ and employed step decay to decrease the learning rate by half after every 10 epochs. We use gradient clipping to clip the values of the gradients above 0.5 and set the clipping norm to a value of 1. We plot the training accuracy, training loss, validation accuracy and validation loss curves for every fold. The total number of parameters in the model were 55,357,729, of which 55,323,297 were trainable and 34,432 were non-trainable. We trained the model for 100 epochs and set the batch size to 8.

For the first fold, the training accuracy reaches 97.83% while the validation accuracy reaches 96.56% after first five epochs. The training accuracy was 100% while the validation accuracy was 99.30% at the hundredth epoch. For the second fold, the training accuracy reaches 97.71% while the validation accuracy reaches 88.12% after first five epochs. The training accuracy was 100% while the validation accuracy was 98.91% at the hundredth epoch. For the third fold, the training accuracy reaches 98.07% while the validation accuracy reaches 95.08% after first five epochs. The training accuracy was 100% while the validation accuracy was 99.06% at the hundredth epoch. For the fourth fold, the training accuracy reaches 98.16% while the validation accuracy reaches 95.94% after first five epochs. The training accuracy was 100% while the validation accuracy was 98.91% at the hundredth epoch. For the fifth fold, the training accuracy reaches 98.03% while the validation accuracy reaches 96.72% after first five epochs. The training accuracy was 100% while the validation accuracy was 99.45% at the hundredth epoch.

Xception Model

We use binary cross-entropy as a loss function and SGD as the optimization algorithm. We set the initial learning rate of SGD to 10⁻⁴ and employed step decay to decrease the learning rate by half after every 10 epochs. We use gradient clipping to clip the values of the gradients above 0.5 and set the clipping norm to a value of 1. We plot the training accuracy, training loss, validation accuracy and validation loss curves for every fold. The total number of parameters in the model were 73,290,793, of which 73,236,265 were trainable and 54,528 were non-trainable. We trained the

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model for 100 epochs except for the first fold which was trained for 200 epochs. We set the batch size to 8.

For the first fold, the training accuracy reaches 100% while the validation accuracy reaches 97.81% at the 200th epoch. For the second fold, the training accuracy reaches 100% while the validation accuracy reaches 97.97% at the hundredth epoch. For the third fold, the training accuracy reaches 99.98% while the validation accuracy reaches 97.66% at the hundredth epoch. For the fourth fold, the training accuracy reaches 100% while the validation accuracy reaches 98.44% at the hundredth epoch. For the fifth fold, the training accuracy reaches 100% while the validation accuracy reaches 97.97% at the hundredth epoch.

Discussion

For both models, selective training/validation set accuracy and training/validation loss plots for different folds are shown in Fig. 4, Fig. 5, Fig. 6, and Fig. 7.

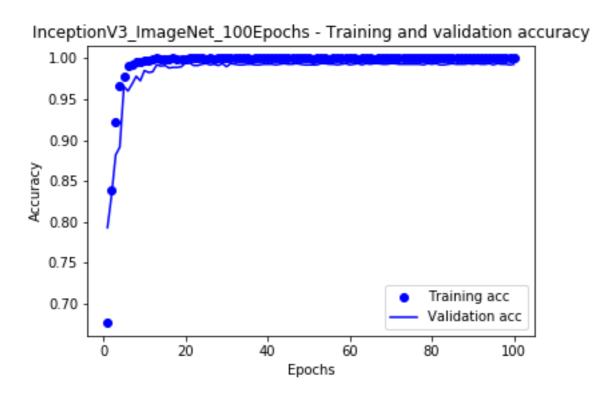


Fig. 4 Accuracy plot for fold 1

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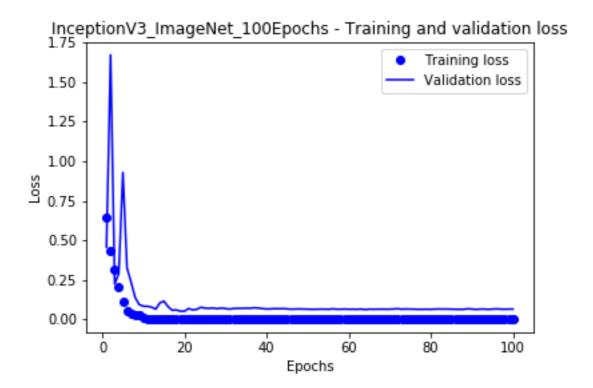


Fig. 5 Loss plot for fold 2

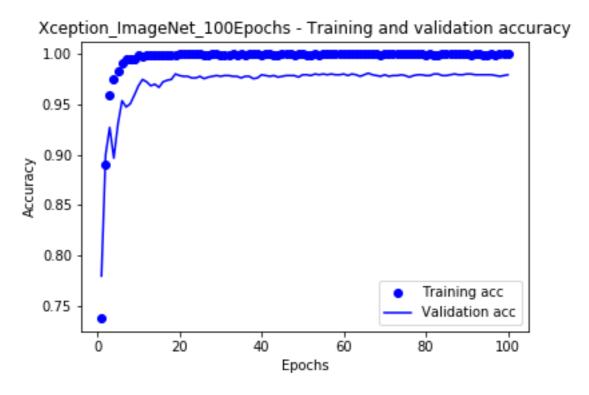


Fig. 6 Accuracy plot for fold 5

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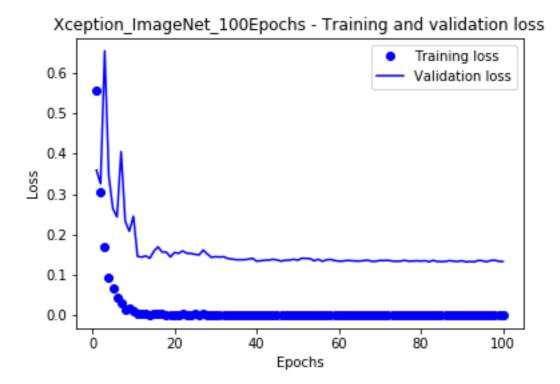


Fig. 7 Loss plot for fold 2

For Inception version 3 model, the plots for training/validation accuracy and losses in all folds are similar to Fig. 4 and Fig. 5 while for the Xception model, the plots for training/validation set accuracy and loss curves for all folds are like Fig. 6 and Fig. 7. We can clearly see a pattern in these curves. The training/validation set accuracies increases with every passing epoch while the loss decreases. The gap in the loss curves for the Xception model is bigger than that in the Inception version 3 model which can be described by small dataset size for training for a model as extreme as Xception. In addition, there are ripples in all curves which represents the learning of gradients by SGD algorithm.

We can clearly see the advantages of using transfer learning for the present task as a small dataset can result in a decent system for the detection of AD.

Comparison with other methods

We compare our results with six recent methods, five of which are based on deep learning, Wavelet [21] is the only non-deep learning based method. For all these

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methods, we compare the average accuracy and the training set size used to achieve that accuracy.

Table 1 Comparison with the State-of-the-art in terms of accuracy and training size

Model	Average Accuracy (%)	Training Size (# of Images)
Wavelet [21]	90.06	3,629
DeepAD (Inception) [22]	98.84	46,751
3DConv [23]	95.39	117,708
Sparse autoencoder [24]	94.74	103,683
Stacked autoencoders [25]	87.76	21,726
Inception version 4 [18]	96.25	5,120
Inception version 3 (Transfer Learning)	99.126	5,120
Xception (Transfer Learning)	97.97	5,120

For our models, we obtain the average accuracy by averaging the validation set accuracies at the hundredth epoch. As can be seen in the table, our Inception version 3 model outperforms every other method while our Xception model comes after DeepAD (Inception) in terms of average accuracy. One reason for lower performance of Xception model can be the number of training parameters present in the network which lead to slight overfitting of the training data during training. The most promising aspect of our models is the number of training samples used which are lower than most of the other models which shows the power of transfer learning for this task. It frees the method from dependence on large tediously annotated training data and improves the training computational time significantly.

Conclusion

To conclude, we show the power of transfer learning for the AD classification task. We present two deep learning models pretrained on imagenet database of images named Inception version 3 and Xception and show their effectiveness in classifying the images on a small dataset. We found the performance of Inception version 3 model to be better than other machine and deep learning models reported in the

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literature. The performance of xception model was a bit inferior due to overfitting of model parameters on a smaller dataset.

As a future work, we will explore other datasets and imaging modalities such as functional MRI, PET etc and multiclass classification problem of AD comprising of healthy control subjects, mild cognitive impairment (MCI) subjects and AD subjects with higher CDR rating. We will also explore more holistic approaches to this problem such as exploring new network architectures, tweaking model parameters such as optimization algorithms, as well as getting insights to the learning of different layers of neural network architectures through different visualization approaches.

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